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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/738,413	12/17/2003	Ralph R. Binetti	SC66U-US	8915

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AVON PRODUCTS, INC.
AVON PLACE
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EXAMINER	
BOWMAN, AMY HUDSON	
ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
06/23/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATENT.DEPARTMENT@AVON.COM

Office Action Summary	Application No.	Applicant(s)	
	10/738,413	BINETTI ET AL.	
	Examiner	Art Unit	
	AMY H. BOWMAN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) ___ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed 4/29/08 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 12/7/07 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-30 are pending in the instant application.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/29/08 has been entered.

This application contains subject matter in the claims that is not directed to the elected sequences, SEQ ID NOs: 1 and 2, which is drawn to an invention nonelected without traverse in the reply filed on 8/22/05. This subject matter is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/22/05.

Applicant's arguments and/or amendments field on 4/29/08, with respect to the rejection under 35 USC 112, 1st paragraph (enablement) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn.

However, the rejections under 35 USC 112, 1st paragraph (written description), 35 USC 102, and 35 USC 103, are pending, as addressed below; and upon further consideration, a new grounds of rejection is applied as set forth below.

Response to Arguments--Claim Rejections - 35 USC § 112

Claims 1-3 and 5-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Applicant acknowledges that applicants cited incorrect GenBank accession numbers for the human and mouse tyrosinase sequences in the reply filed on 10/9/07. Although applicant argues that the sequences that are intended to be the instant tyrosinase sequences are those that are disclosed by Bennett et al. (US 2004/0215006 A1), this does not meet the written description requirement. Bennett et al. discloses three different mouse tyrosinase sequences (GenBank accession number NM_011661.1, GenBank accession number X51743.1, and GenBank accession number D00131.1) (see page 21 of Bennett et al.), thus supporting that the term "tyrosinase" embraces a genus of sequences, a genus that has not been defined.

The instant claims are directed to administering only those siRNA molecules that target both mouse and human tyrosinase, although applicant has not closed mouse or human "tyrosinase" to any single sequence in the claims. The instant specification

discloses three sequences that are "homologous to sequences found in both human and mouse forms of tyrosinase". It is noted that although applicant is claiming a method involving only the specific subset of siRNAs that target both mouse and human tyrosinase mRNA, the human and mouse mRNA sequences have not been defined by applicant in a way that would allow for one of ordinary skill to envision which siRNA oligomers are directed to both sequences without further knowledge of the specific target sequences because "tyrosinase", as instantly claimed can encompass any mouse or human tyrosinase sequence, as well as encompass any mouse or human tyrosinase homolog or allele known or yet to be discovered of mouse or human tyrosinase, as well as DNA genomic fragments, spliced variants or fragments that retain mouse or human tyrosinase-like activity.

One of ordinary skill in the art could not envision the member siRNAs of the instant method that are targeted to both human and mouse tyrosinase mRNA without knowledge of the target sequences in order to define which area of the sequences are homologous and which are not. Therefore, one would not be able to recognize that the applicant was in possession of the claimed genus at the time of filing.

Response to Arguments---Claim Rejections - 35 USC § 102

Claims 1-3, 5-9, 14 and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Bennett et al. (US 2004/0215006 A1) (of record and first cited by the examiner in the office action mailed on 7/10/07).

The invention of the above claims is drawn to methods of inhibiting the production of melanin in a human comprising topically administering to the skin of the human a composition comprising a siRNA having a sequence complementary to a sequence found in mouse and native human tyrosinase mRNA, said siRNA comprising two strands, each of said strands having between 15 and 21 nucleotides, including two thymidine nucleotide overhangs, said composition comprising an amount of said siRNA oligomer effective to reduce production of melanin. The skin suffers from hyperpigmentation. The invention is further directed to specific dosing and delivery requirements.

Bennett et al. teach methods of modulating the expression of tyrosinase in cells, tissues, or animals comprising contacting said cells, tissues, or animals with one or more of the compounds or compositions of the invention. Bennett et al. teach methods of treating an animal, particularly a human, suspected of having or being prone to a disease or condition associated with expression of tyrosinase (see page 2, paragraph 0016, for example). Bennett et al. teach that the compounds of the invention can be single or double stranded antisense oligonucleotides (see page 3, paragraphs 0025 and 0026; and example 5).

Bennett et al. teach that the color of mammalian skin and hair is determined largely by the degree and distribution of melanin production and teach that the involvement of tyrosinase in melanoma make its selective inhibition an appropriate point for therapeutic intervention in these disorders (see page 1). Bennett et al. teach that antisense oligonucleotides pointed to tyrosinase in skin cosmetics have been used to

beautify and whiten the skin and teach that antisense oligonucleotides targeting the tyrosinase gene have been used as depigmentation or skin whitening agents in a cosmetic composition or a dermatologic composition (see page 1). Bennett et al. teach that antisense molecules demonstrated to reduce levels of tyrosinase in melanocytes have therapeutic potential to treat several diseases of hyperpigmentation (see paragraph [0010]).

Bennett et al. specifically teach that the compounds of the invention can be formulated in topical formulations and that administration may be topical. The topical formulations of Bennett et al. such as lotions and creams are taught to be administered topically and would therefore necessarily be applied to some portion of the face, forehead, neck, arms, hands, legs, knees, feet, chest, back, groin, or buttocks, as instantly recited. Bennett et al. teach that pharmaceutical compositions and formulations for topical administration may include transdermal patches, ointments, lotions, creams, gels, drops, suppositories, sprays, liquids and powders. Conventional carriers may also be incorporated (see page 10). Bennett et al. teach that preferred formulations for topical administration include those in which the oligonucleotides are in admixture with a topical delivery agent such as lipids and liposomes (see page 11). The instant specification does not define “biodegradable microsphere”, as recited in instant claim 26. The liposomes and delivery agents of Bennett et al. are considered to meet this instant limitation.

Bennett et al. teach various dosing parameters and teach that generally dosage is from 0.01 ug to 100 g per kg of body weight, and may be given once or more daily, weekly, monthly or yearly, or even once every 2 to 20 years (see page 12).

The instant specification does not define what is meant by "sensitive skin", as recited in instant claim 18. The subjects being treated by the method of Bennett et al. for a tyrosinase related disorder such as melanoma are considered to have sensitive skin, as instantly recited.

Bennett et al. disclose that duplexes of the invention comprise an antisense strand that comprises at least a portion of an oligonucleotide in Table 1 (see Example 5, page 14). Table 1 discloses multiple oligonucleotides, or antisense strand sequences, that target a human tyrosinase sequence and Table 2 discloses antisense strand sequences that target a mouse tyrosinase sequence. However, since there is a degree of overlap between the tyrosinase sequences utilized by Bennett et al., there is an antisense sequence that targets both. For example, SEQ ID NO: 27 in Table 1 of Bennett et al. is 20 nucleotides in length and targets the human tyrosinase sequence disclosed by Bennett et al. at position 1609. This oligonucleotide targets both the human and mouse sequences disclosed by Bennett et al. (starting at position 1609 of the human sequence disclosed as GenBank M27160.1 by Bennett et al. and starting at position 1168 of the mouse sequence disclosed as GenBank NM_011661.1 by Bennett et al.). Therefore, although Bennett et al. lists oligonucleotide sequences in a human table and in a mouse table, Bennett et al. discloses oligonucleotides that may target both sequences and teaches that duplexes of the invention comprise the sequences or

portions of the sequences in table 1. Neither Bennett et al. nor the instant specification disclose a structure to define which molecules would be targeted to both sequences. However, Bennett et al. discloses SEQ ID NO: 27 that is complementary to both and thus anticipates the instant siRNA of the instant method.

Applicant asserts that an siRNA comprising SEQ ID NO: 27 of Bennett et al. would not anticipate the instant claims because SEQ ID NO: 27 is 20 nucleotides in length and therefore the addition of a two nucleotide overhang, as required by the instantly amended claims, would result in a siRNA that is 22 nucleotides in length.

Contrary to applicant's assertion, the instant claims are not closed to siRNA oligomers that are between 15 and 21 nucleotides in length, as the instant claims recite "having" between 15 and 21 nucleotides, which is open language. Therefore, the resultant siRNA of Bennett et al. would have 21 nucleotides plus an additional one nucleotide, which is not excluded from the instant claim language.

Furthermore, as explained above, Bennett et al. does not require for the oligomer to be the full length that is exemplified in the tables but rather discloses that duplexes of the invention comprise an antisense strand that comprises "at least a portion of an oligonucleotide in Table 1" and therefore embrace smaller oligomers that are consistent with the teachings of the specification, which discloses various sizes in paragraph [0029], for example. Bennett et al. teaches that the duplexes can have a two-nucleobase overhang (see paragraph [0139]).

Applicant argues that there would be no motivation to target 15-21 consecutive nucleotides of an RNA region commonly shared by mouse and human based on the

disclosure of Bennett et al. because Bennett et al. separately considers targeting mouse and human sequences of tyrosinase. It is noted that motivation is not a consideration of a rejection under 35 USC 102. Bennett et al. teaches a method comprising the instant method steps with dsRNA molecules that meet the instant structural limitations, including that of having the required complementarity to a human and a mouse tyrosinase sequence.

Motivation is a consideration of a rejection under 35 USC 103(a). However, in the instant case, the primary reference teaches a method comprising the instant method steps with dsRNA molecules that meet the instant structural limitations, including that of having the required complementarity to a human and a mouse tyrosinase sequence. Therefore, the only motivation needed is that of combining Bennett et al. with the other references, rather than a motivation for what is taught by Bennett et al.

Response to Arguments---Claim Rejections - 35 USC § 103

Claims 1-3 and 5-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett et al. (US 2004/0215006 A1), in view of Mahashabde et al. (US 6,436,378 B1), and Perricone (US 2002/0141956 A1) (each of the references are of record and first cited by the examiner in the office action mailed on 7/10/07).

Applicant has not offered any arguments regarding this rejection that have not been directly addressed in the rejection under 35 U.S.C. 102 (Bennett et al.) above.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

New Objections/Rejections

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett et al. (US 2004/0215006 A1), in view of Mahashabde et al. (US 6,436,378 B1),

Perricone (US 2002/0141956 A1) (each of the references are of record and first cited by the examiner in the office action mailed on 7/10/07), and Ambion siRNA target finder (http://www.ambion.com/techlib/misc/siRNA_finder.html, available 2002 to the public). .

The invention of the above claims is drawn to methods of inhibiting the production of melanin in a human comprising topically administering to the skin of the human a composition comprising a siRNA having a sequence complementary to a sequence found in mouse and native human tyrosinase mRNA, said siRNA comprising two strands, each of said strands having between 15 and 21 nucleotides, including two thymidine nucleotide overhangs, said composition comprising an amount of said siRNA oligomer effective to reduce production of melanin. The skin suffers from hyperpigmentation. The invention is further directed to specific dosing and delivery requirements; and wherein the siRNA oligomer is SEQ ID NOs: 1 and 2.

Bennett et al. teach methods of modulating the expression of tyrosinase in cells, tissues, or animals comprising contacting said cells, tissues, or animals with one or more of the compounds or compositions of the invention. Bennett et al. teach methods of treating an animal, particularly a human, suspected of having or being prone to a disease or condition associated with expression of tyrosinase (see page 2, paragraph 0016, for example). Bennett et al. teach that the compounds of the invention can be single or double stranded antisense oligonucleotides (see page 3, paragraphs 0025 and 0026; and example 5).

Bennett et al. teach that the color of mammalian skin and hair is determined largely by the degree and distribution of melanin production and teach that the

involvement of tyrosinase in melanoma make its selective inhibition an appropriate point for therapeutic intervention in these disorders (see page 1). Bennett et al. teach that antisense oligonucleotides pointed to tyrosinase in skin cosmetics have been used to beautify and whiten the skin and teach that antisense oligonucleotides targeting the tyrosinase gene have been used as depigmentation or skin whitening agents in a cosmetic composition or a dermatologic composition (see page 1). Bennett et al. teach that antisense molecules demonstrated to reduce levels of tyrosinase in melanocytes have therapeutic potential to treat several diseases of hyperpigmentation (see paragraph [0010]).

Bennett et al. specifically teach that the compounds of the invention can be formulated in topical formulations and that administration may be topical. The topical formulations of Bennett et al. such as lotions and creams are taught to be administered topically and would therefore necessarily be applied to some portion of the face, forehead, neck, arms, hands, legs, knees, feet, chest, back, groin, or buttocks, as instantly recited. Bennett et al. teach that pharmaceutical compositions and formulations for topical administration may include transdermal patches, ointments, lotions, creams, gels, drops, suppositories, sprays, liquids and powders. Conventional carriers may also be incorporated (see page 10). Bennett et al. teach that preferred formulations for topical administration include those in which the oligonucleotides are in admixture with a topical delivery agent such as lipids and liposomes (see page 11). The instant specification does not define "biodegradable microsphere", as recited in instant

claim 26. The liposomes and delivery agents of Bennett et al. are considered to meet this instant limitation.

Bennett et al. teach various dosing parameters and teach that generally dosage is from 0.01 ug to 100 g per kg of body weight, and may be given once or more daily, weekly, monthly or yearly, or even once every 2 to 20 years (see page 12).

The instant specification does not define what is meant by "sensitive skin", as recited in instant claim 18. The subjects being treated by the method of Bennett et al. for a tyrosinase related disorder such as melanoma are considered to have sensitive skin, as instantly recited.

Bennett et al. disclose that duplexes of the invention comprise an antisense strand that comprises at least a portion of an oligonucleotide in Table 1 (see Example 5, page 14). Table 1 discloses multiple oligonucleotides, or antisense strand sequences, that target a human tyrosinase sequence and Table 2 discloses antisense strand sequences that target a mouse tyrosinase sequence. However, since there is a degree of overlap between the tyrosinase sequences utilized by Bennett et al., there is an antisense sequence that targets both. For example, SEQ ID NO: 27 in Table 1 of Bennett et al. is 20 nucleotides in length and targets the human tyrosinase sequence disclosed by Bennett et al. at position 1609. This oligonucleotide targets both the human and mouse sequences disclosed by Bennett et al. (starting at position 1609 of the human sequence disclosed as GenBank M27160.1 by Bennett et al. and starting at position 1168 of the mouse sequence disclosed as GenBank NM_011661.1 by Bennett et al.). Therefore, although Bennett et al. lists oligonucleotide sequences in a human

table and in a mouse table, Bennett et al. discloses oligonucleotides that may target both sequences and teaches that duplexes of the invention comprise the sequences or portions of the sequences in table 1. Neither Bennett et al. nor the instant specification disclose a structure to define which molecules would be targeted to both sequences. However, Bennett et al. discloses SEQ ID NO: 27 that is complementary to both and thus anticipates the instant siRNA of the instant method.

Applicant asserts that an siRNA comprising SEQ ID NO: 27 of Bennett et al. would not anticipate the instant claims because SEQ ID NO: 27 is 20 nucleotides in length and therefore the addition of a two nucleotide overhang, as required by the instantly amended claims, would result in a siRNA that is 22 nucleotides in length.

Contrary to applicant's assertion, the instant claims are not closed to siRNA oligomers that are between 15 and 21 nucleotides in length, as the instant claims recite "having" between 15 and 21 nucleotides, which is open language. Therefore, the resultant siRNA of Bennett et al. would have 21 nucleotides plus an additional one nucleotide, which is not excluded from the instant claim language.

Furthermore, as explained above, Bennett et al. does not require for the oligomer to be the full length that is exemplified in the tables but rather discloses that duplexes of the invention comprise an antisense strand that comprises "at least a portion of an oligonucleotide in Table 1" and therefore embrace smaller oligomers that are consistent with the teachings of the specification, which discloses various sizes in paragraph [0029], for example. Bennett et al. teaches that the duplexes can have a two-nucleobase overhang (see paragraph [0139]).

Bennett et al. does not teach for the composition to comprise a sunscreen, such as octylmethoxycinnamate, and does not teach alpha hydroxy acid. Bennett et al. does not teach instant SEQ ID NOs: 1 and 2 as a siRNA.

Mahashabde et al. teach a composition comprising a cream or lotion base said base further comprising a) an active agent or mixture thereof which brings about skin lightening, and b) an active agent or mixture thereof which prevents skin from further darkening when exposed to ultraviolet light (see abstract and claim 1). Mahashabde et al. teach that the agent to lighten skin can be those which can inhibit the synthesis of melanin such as tyrosinase inhibitors and that the agent to prevent further darkening when exposed to UV light can be a sunscreen such as octylmethoxycinnamate (OMC) (see column 1).

Perricone teaches a method for whitening skin comprising topically administering to the skin a composition comprising alpha hydroxy acid (see claims 1 and 7). Perricone teaches that some embodiments of the skin whitening composition contain adjunct ingredients that enhance the efficacy and stability of skin whitening formulations such as a tetronic acid derivative that inhibits tyrosinase (see abstract).

Ambion teaches a siRNA target finder and design tool and teaches that the algorithms followed the guidelines for siRNA design to generate a report indicating preferential sense and antisense siRNA oligonucleotides for a given mRNA sequence. Upon entry of a human tyrosinase sequence (GenBank accession number M27160.1) into the Ambion tool, a siRNA that is 100% identical to instant SEQ ID NOs: 1 and 2 was generated, including the two nucleotide 3'-overhangs.

It would have been obvious to incorporate a sunscreen, such as octylmethoxycinnamate, as taught by Mahashabde et al. or alpha hydroxy acid, as taught by Perricone, into the composition of the method of Bennett et al.

It would have been obvious to utilize the specific siRNA consisting of instant SEQ ID NOs: 1 and 2, as taught by Ambion, in the method of Bennett et al.

One would have been motivated to incorporate a sunscreen, such as octylmethoxycinnamate, as taught by Mahashabde et al. or alpha hydroxy acid, as taught by Perricone, into the composition of the method of Bennett et al. because Bennett et al. teach a method of topically administering a composition comprising one or more siRNA molecules (double stranded oligonucleotides) targeted to tyrosinase mRNA to modulate the expression of tyrosinase in cells and thereby treat a human in need thereof. Therefore, one would have been motivated to optimize the method by incorporating other agents that were known in the art to achieve the same benefit of treating a tyrosinase disorder or lightening skin pigmentation.

Since Mahashabde et al. teach a composition comprising a) an active agent or mixture thereof which brings about skin lightening, such as a tyrosinase inhibitor and b) an active agent or mixture thereof which prevents skin from further darkening when exposed to ultraviolet light, such as octylmethoxycinnamate (OMC), one would have been motivated to combine OMC with the tyrosinase inhibitor of Bennett et al. to achieve the same benefit.

Furthermore, one would have been motivated to incorporate alpha hydroxy acid into the composition of the method of Bennett et al. because Perricone teaches a

method for whitening skin comprising topically administering to the skin a composition comprising alpha hydroxy acid. Perricone teaches that some embodiments of the skin whitening composition contain adjunct ingredients that enhance the efficacy and stability of skin whitening formulations such as a tetronic acid derivative that inhibits tyrosinase (see abstract).

One would have been motivated to specifically design the siRNA targeted to tyrosinase to consist of instant SEQ ID NOs: 1 an 2 because Ambion teaches an algorithm, wherein insertion of a human tyrosinase sequence results in the identification of hotspots and preferential siRNA sequences and specifically identified a preferred siRNA that is 100% identical to instant SEQ ID NOs: 1 and 2.

Since both Mahashabde et al. and Perricone teach beneficial ingredients for compositions that lighten skin pigmentation and each teach that these compositions can also comprise tyrosinase inhibitors, one would have had a reasonable expectation of success given that Bennett et al. teaches a method comprising administering a topical siRNA directed to tyrosinase that the ingredients of Mahashabde et al. and Perricone would further optimize the outcome of the method of Bennett et al.

Furthermore, since Bennett et al. teaches a method with each of the instant method steps, one would have had a reasonable expectation of success of utilizing a specific siRNA that is identified by the Ambion algorithm, the algorithm of which is designed to identify preferable siRNA molecules given a target sequence, wherein the target sequence was already targeted with nucleic acid inhibitory molecules specific for tyrosinase, as evidenced by Bennett et al.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMY H. BOWMAN whose telephone number is (571)272-0755. The examiner can normally be reached on Monday-Thursday 6:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amy H. Bowman/
Examiner, Art Unit 1635